

CLAIMS

✓. Use of ubiquicidine or optionally modified peptide fragments derived therefrom for the preparation of a drug for the treatment, diagnostics or prophylaxis of infections in humans and animals.

5 2. Peptide fragment derived from ubiquicidine and comprising a continuous series of at least 3 amino acids from the amino acid sequence of ubiquicidine:
KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVVPTFGKKGPNA
NS, with the exception of peptides having the amino acid 10 sequence KVHGSLARAGKVRGQTPKVAKQ or AGKVRGQTPKVAKQEKKKKKT.

15 3. Peptide fragment as claimed in claim 2 comprising a continuous series of at least 8 amino acids from the amino acid sequence of ubiquicidine:

KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVVPTFGKKGPNA
NS, with the exception of peptides having the amino acid 20 sequence KVHGSLARAGKVRGQTPKVAKQ or AGKVRGQTPKVAKQEKKKKKT.

4. Peptide fragment as claimed in ^{Claim 2} ~~claims 2~~ and 25 with one of the following amino acid sequences:

ubiquicidine (1-18)	KVHGSLARAGKVRGQTPK
ubiquicidine (29-41)	TGRAKRRMQYNRR
ubiquicidine (18-29)	KVAKQEKKKKKT
ubiquicidine (18-35)	KVAKQEKKKKKTGRAKRR
ubiquicidine (29-35)	TGRAKRR
ubiquicidine (42-59)	FVNVVPTFGKKGPNA
ubiquicidine (36-41)	NS, MQYNRR

5. Derivative of ubiquicidine or of a peptide fragment derived from ubiquicidine and comprising a continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine:

30 KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVVPTFGKKGPNA NS, which derivative has an amino acid sequence which is at least partly the reverse of the amino acid sequence of the corresponding original peptide (fragment) (so-called "partial) reverse peptide").

35 6. Derivative of a ubiquicidine or of a peptide fragment derived from ubiquicidine and comprising a

continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine: KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVPTFGKKGPNA

NS, wherein at least one of the amino acids from the original peptide (fragment) is replaced by a stereoisomer of that amino acid.

7. Derivative of ubiquicidine or of a peptide fragment derived from ubiquicidine and comprising a continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine: KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVPTFGKKGPNA NS, wherein the original amino acid chain is extended at one or both ends thereof with one or more groups, such as D-amino acids, protecting against degradation.

8. Derivative as claimed in claim 7 with the amino acid sequence:

D-A--KVAKQEKKKKKTGRAKRR--D-A
in which D-A represents D-alanine.

9. Hybrid molecule, comprising a cationic peptide with an antimicrobial action and/or a peptide fragment as claimed in claims 2-4 and/or a derivative thereof as claimed in claims 5-8, and one or more effector molecules.

10. Hybrid molecule as claimed in claim 9, wherein the effector molecule comprises an amino acid chain which is capable of binding to a micro-organism and/or substances secreted by micro-organisms or expressed on the surface thereof.

11. Hybrid molecule as claimed in claim 9, wherein the effector molecule is an endotoxin-binding peptide.

12. Hybrid molecule as claimed in claim 9, wherein the effector molecule is a detectable label.

13. Hybrid molecule as claimed in claim 12, wherein the detectable label is a radionuclide chosen from the group consisting of technetium 99m (Tc-99m), iodine 123 (I-123) and 131 (I-131), bromine 75 (B-75) and 76 (B-76), lead 203 (Pb-203), gallium 67 (Ga-67) and 68

(Ga-68), arsenic 72 (As-72), indium 111 (In-111), 113m (In-113m) and 114m (In-114m), ruthenium 97 (Ru-97), copper 62 (Cu-62), 64 (Cu-64) and 67 (Cu-67), iron 52 (Fe-52), manganese 52m (Mn-52m), chromium 51 (Cr-51),

5 rhenium 186 (Re-186) and 188 (Re-188), terbium 161 (Tb-161), yttrium 90 (Y-90), fluorine 19 (F-19), sodium 23 (Na-23), phosphorus 31 (P-31), gadolinium 157 (Gd-157), manganese 55 (Mn-55), dysprosium 162 (Dy-162), chromium 52 (Cr-52) and iron 56 (Fe-56).

10 14. Hybrid molecule as claimed in claim 9, wherein the cationic peptide with antimicrobial activity is chosen from α - and β -defensins, ubiquicidine, protegrins, serprocidins, magainins, PR-39, cecropins.

15 15. A peptide fragment derived from ubiquicidine and comprising a continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine:
KVGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVPFGKKGPNA
NS for use in the diagnostics, prophylaxis or therapy of infections in humans and animals.

20 16. Peptide fragments as claimed in claim 3 for use in the diagnostics, prophylaxis or therapy of infections in humans and animals.

25 17. Derivatives as claimed in claims 5-8 for use in the diagnostics, prophylaxis or therapy of infections in humans and animals.

18. Hybrid molecules as claimed in claims 9-14 for use in the diagnostics, prophylaxis, therapy or monitoring of infections in humans and animals.

30 19. Peptide fragments as claimed in claim 15 or 16, derivatives as claimed in claim 17 or hybrid molecules as claimed in claim 18, wherein the microbial infections are caused by pathogenic Gram-positive (Staphylococcus aureus, Listeria monocytogenes including antibiotic-resistant strains of S.aureus (also called Multidrug Resistant S.aureus (MRSA)) and Gram-negative ((antibiotic-resistant) Klebsiella pneumoniae, Escherichia coli, enterococci and Salmonella typhimurium)

bacteria, micro-organisms difficult to treat, such as Mycobacterium avium and Mycobacterium fortuitum, fungi, such as Candida albicans, Cryptococcus neoformans and Aspergillus fumigatis, viruses, in particular enveloped viruses, and parasites, such as Trypanosoma cruzi and Toxoplasma gondii.

20. Antimicrobial agent, comprising at least a suitable quantity of one or more active components chosen from ubiquicidine, peptide fragments derived from 10 ubiquicidine and comprising a continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine:

KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVN
NS, derivatives thereof as claimed in claims 5-8, hybrid 15 molecules as claimed in claims 9-14, optionally in the presence of one or more suitable excipients.

21. Antimicrobial agent as claimed in claim 20 for use in therapy and prophylaxis in humans and animals.

22. Diagnostic agent, comprising a suitable 20 quantity of one or more active components provided with a detectable label and chosen from ubiquicidine, peptide fragments derived from ubiquicidine and comprising a continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine:
KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVN
NS, derivatives thereof as claimed in claims 5-8, hybrid 25 molecules as claimed in claims 9-14.

23. Diagnostic agent as claimed in claim 20 for use in diagnostics and monitoring.

30 24. Method for labelling a cationic peptide with antimicrobial action, comprising of placing the peptide for labelling in contact with a tin(II) salt, a borohydride and a radioactive label in the presence of alkali, wherein the peptide is modified with MAG3 (mercapto-acetyl glycine-glycine).

35 25. Method as claimed in claim 24, wherein the tin(II) salt and the borohydride are respectively tin-(II) pyrophosphate and sodium borohydride or potassium

borohydride, which are used in a ratio between 1:1 and 1:10, preferably 1:4, in quantities of respectively 0.5-5 µl and 2-10 µl, wherein the radioactive label is a standard solution of ^{99m}Tc-pertechnetate or ¹⁸⁶Re-perrhenate in a quantity of 0.05-0.5 ml, preferably 0.1 ml, wherein the alkali is sodium hydroxide and the alkali concentration is 0.5-5 M, preferably 0.1 M, and wherein the whole is stirred for 1 to 60 minutes, preferably 5 to 30 minutes at a temperature between room temperature and 40°C, and preferably at about 37°C.

26. Method for preparing ubiquicidine, peptide fragments derived from ubiquicidine and comprising a continuous series of at least 3, preferably at least 8 amino acids from the amino acid sequence of ubiquicidine: KVHGSLARAGKVRGQTPKVAKQEKKKKKTGRAKRRMQYNRRFVNVPFGKKKGPNANS, derivatives thereof as claimed in claims 5-8, hybrid molecules as claimed in claims 9-14 by transforming an animal egg-cell with a gene construct which codes for the ubiquicidine, peptide fragment, derivative or hybrid molecule, regenerating a transgenic animal from the transformed egg-cell and isolating the ubiquicidine, peptide fragment, derivative or hybrid molecule from a tissue or bodily fluid of the animal, for instance milk.

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